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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/030,378
Filing Date: November 09, 2001
Appellant(s): BLUE, JEFFREY T.

Sheldon Heber
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 25, 2006 appealing from the Office action mailed February 22, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

This appeal involves claims 1-8 and 18-25.

Claims 9-17 have been canceled.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

The rejection of claims 1-8 and 18-25 under 35 U.S.C. § 112, Second paragraph is withdrawn by the examiner.

The rejection of claims 21 and 24 under 35 U.S.C. § 112, First paragraph, written description requirement, is withdrawn by the examiner. It is noted that the appeal brief, page 7, filed by Appellant does not address this rejection.

Additionally, it is noted that the rejection of claims 4-5 and 18-19 under 35 U.S.C § 103 (a) as obvious over Banki et al. in view of Duncan et al. inadvertently omitted to list claims 21 and 24. However, the limitations of claims 21 and 24 were addressed in the rejection. This inadvertent omission is corrected below. It should be noted that no new grounds of rejection is added.

In addition, it is noted that the rejection of claims 1, 20, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., in view of Wu et al. inadvertently omitted to list Duncan et al. However, it is clear from the record that the teachings of Duncan et al. are relied upon for the rejection. This inadvertent omission is corrected below. It should be noted that no new grounds of rejection is added.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

- Banki et al. Molecular ordering in HIV-induced apoptosis. The Journal of Biological Chemistry. May 08, 1998; Vol. 273, No. 19, 11944-11953.

- Duncan et al. Rubella virus-induced apoptosis varies among cell lines and is modulated by Bcl-XI and caspase inhibitors. Virology, March 01, 1999, Vol. 255, 117-128.
- Wu et al. U.S. Patent No. 6,689,600, which claims priority to U.S. Provisional No. 60/108606, which was filed November 16, 1998, [lines 5-10, page 3].
- Goodrich, Jr. et al. U.S. Patent No. 5,958,670, filed June 15, 1994.
- Esolen et al. Apoptosis as a cause of death in measles virus-infected cells. Journal of Virology, 1995, Vol. 96, No. 6, 3955-3958.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

I. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Banki et al.[1]

In the instant, the claims are directed to a process comprising the following active steps:

a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, and

b) measuring said caspase 3 activity, wherein steps a) and b) are repeated at two or more time intervals. The claims also require that the caspase 3 activity be measured using a caspase 3 substrate linked to a fluorimetric or colorimetric moiety, wherein the substrate is Asp-Glu-Val-Asp (DEVD).

Banki et al. teaches a process comprising the following active steps:

a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, and

b) measuring said caspase 3 activity, wherein steps a) and b) are repeated at two or more time intervals. [See particularly Figure 2 with caption, page 11946; 1st sentence, last full paragraph, page 11948; and Figure 5 with caption, page 11949]

Banki et al. measured caspase 3 activity using a caspase 3 substrate linked to a fluorimetric or colorimetric moiety, wherein the substrate is Asp-Glu-Val-Asp (DEVD).

In the instant, Banki et al. teaches the claimed invention. The claimed invention is directed at a method for measuring caspase 3 activity. And Banki et al. teaches a method of measuring caspase 3 activity. The method of Banki et al. is the same as those recited in the claims. Thus, Banki et al. teaches the claimed method. Therefore, Banki et al. anticipates the claimed invention.

Furthermore, the recitation "provides an indication of virus stability and potency" and derivation thereof do not state a condition that is material to patentability; thus, is not given weight. The cited recitation simply expresses the intended result of a process. Thus, Banki et al. does not need to express an intention or purpose that is the same as those recited in the claims to render the claims unpatentable. See MPEP § 2114.04, which states: Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure...The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v.

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[1] Banki et al. Molecular ordering in HIV-induced apoptosis. The Journal of Biological Chemistry. May 08,

Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." Id. However, the court noted (quoting Minton v. Nat 'l Ass 'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'" Id.

Therefore, for the reasons set for above, Applicant's submission is not found persuasive. The claims remain anticipated by Banki et al.

II. Claims 4-5, 18-19, 21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claims 1-3, in view of Duncan et al.[2]

Claims 4-5, 18-19, 21 and 24 limit the virus to measles, mumps or rubella virus; and the cells to Vero or RK-13 cells.

The relevance of Banki et al. as it pertains to claims 1-3 is discussed above.

Duncan et al. teaches that that rubella virus induces apoptosis in Vero and RK13 cells. To quantify rubella virus induced apoptosis, Duncan et al. quantified the number of detached cells as an indicator of apoptosis.

Duncan et al. does not teach the measurement of caspase 3 activity as an alternative procedure to quantify virally induced apoptosis, as provided by Banki et al.

1998; Vol. 273, No. 19, 11944-11953.

[2] Duncan et al. Rubella virus-induced apoptosis varies among cell lines and is modulated by Bcl-Xl and caspase inhibitors. Virology, March 01, 1999, Vol. 255, 117-128.

Banki et al. teaches the measurement of caspase 3 activity to quantify viral induced apoptosis, as noted above for claims 1-3.

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to combine the teachings of Banki et al. with Duncan et al. One of ordinary skill in the art at the time the invention was made would have been motivated to so to quantify virally induced apoptosis. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the use of caspase 3 activity to quantify virally induced apoptosis is well known in the art.

III. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claims 1-3, in view of Wu et al.[3]

Claim 6 requires that prior to contacting the virus with the cell that the virus be lyophilized.

The relevance of Banki et al. as it pertains to claims 1-3 is discussed above. In the instant, it is not readily apparent if Banki et al. lyophilizes the virus. However, it is noted that Banki et al. does teach storing aliquots of supernatants with viral titers by freezing the aliquots at –70 degrees C.

Wu et al. teaches that lyophilization improves the stability of viral vaccine and recombinant protein products.

Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to lyophilize the virus. One of ordinary skill in the art at

the time the invention was made would have been motivated to do so to improve the stability of the viral supernatant. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the art recognizes that lyophilization improves the stability of viral vaccine and recombinant protein products. Thus, absent evidence to the contrary, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for producing the claimed invention.

IV. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claims 1-3, in view of Goodrich, Jr. et al.

Claim 8 requires that the cells be frozen then thawed.

The relevance of Banki et al. as it pertains to claims 1-3 is discussed above. In the instant, Banki et al. does not teach the freezing and thawing of the cells prior to contacting the cells with the virus.

However, Goodrich et al. does teach a method of storing cells by freezing the cells and later thawing the cells for use.

Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to freeze and thaw the cell. One of ordinary skill in the art at the time the invention was made would have been motivated to freeze the cells to allow storage of the cells, and thaw the frozen cells to use the cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the freezing and thawing of cells is well

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[3] Wu et al. U.S. Patent No. 6,689,600, which claims priority to U.S. Provisional No. 60/108606 [lines 5-10,

recognized in the art as a method of storing cells. Thus, absent evidence to the contrary, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for producing the claimed invention.

V. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claim 18, in view of Esolen et al.[4]

Claim 22, which depends on claim 18, limits the virus to measles or mumps virus.

The relevance of Banki et al. as it pertains to claim 18 is discussed above. Banki et al. teaches a method of measuring caspase 3 activity to quantify virally induced apoptosis. The virus Banki et al. teaches is not measles or mumps. However, the deficiency noted of Banki et al. is compensated by Esolen et al. Esolen et al. teaches that measles virus induces apoptosis.

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to combine the teachings of Banki et al. and Esolen et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to quantify apoptosis induced by the measles virus. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the use of caspase 3 activity to quantify virally induced apoptosis is well known in the art.

VI. Claims 1, 20, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., by itself or in view of Duncan et al., in view of Wu et al.

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page 3].

The claims require the measurement of caspase 3 activity be conducted for one virus obtained from two different formulations.

The relevance of Banki et al. by itself or in view of Duncan et al. is discussed above. As noted in the above paragraphs, Banki et al. teaches a method of measuring caspase 3 activity to quantify virally induced apoptosis. The difference between the claimed invention and Banki et al. is that Banki et al. does not measure caspase 3 activity induced by the virus obtained from two different formulations.

However, Wu et al. does teach the significance of formulations on the biological activity and structural integrity of viral particles. [Lines 26-30 of page 2]

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to compare different viral formulations. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to determine the effects of the formulation on the biological activity and structural integrity of the virus. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Banki et al. teaches the measurement of caspase 3 activity to quantify virally induced apoptosis.

(10) Response to Argument

In response to all the art rejections, both anticipatory and obvious, Appellant submits that Banki et al. does not appear to repeat the cell infection step using HIV

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[4] Esolen et al. Apoptosis as a cause of death in measles virus-infected cells. Journal of Virology, 1995, Vol. 96, No. 6, 3955-3958.

obtained from a first formulation at different times. [Last sentence, second full paragraph, page 11 of brief.]

Appellant's submission has been considered, however, the examiner does not find it persuasive. In the instant case, it is not understood how the prior art does not anticipate or render the claimed invention obvious. The claims are directed to a process comprising the following active steps: a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, and b) measuring said caspase 3 activity, wherein steps a) and b) are repeated at two or more time intervals.

Banki et al. teaches a process comprising the following active steps:

- a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity. See a) Infection with HIV-1 section, page 11947; b) 1st sentence, last full paragraph, page 11948; and c) Figure 5 with caption, page 11949 of Banki et al. In the instant case, Banki et al. clearly teaches contacting Jurkat-tat and H9 cells, which are susceptible to caspase 3 induction, with the human immunodeficiency virus, which induces caspase 3 activity.
- b) measuring said caspase 3 activity. See Caspase-3/CCP32 Enzyme Assay and Protease Inhibitors section, page 11947; b) 1st sentence, last full paragraph, page 11948; and c) Figure 5 with caption, page 11949 of Banki et al. In the instant case, Banki et al. measured caspase 3 activity induced by the HIV virus in both Jurkat-tat and H9 cells. In addition to measuring

caspase-3 activity at time zero, Banki et al. also measured caspase-3 activity at day 2, 4, 6 and 8—as shown in Figure 2; and at day 2, 4 and 7—as shown in Figure 5. Thus, not only did Banki measure caspase-3 activity at one time interval, Banki et al. also measured caspase-3 activity at several time intervals.

- Repeating steps a) and b) at two or more time intervals. See last sentence of caption provided for Figures 2 and 5, pages 11946 and 11949, respectively, of Banki et al. In the instant case, Banki et al. teaches repeating steps a) and b) with both HIV infected Jurkat-tat and H9 cells three different times in order to present the data in mean standard error form. Like above, in addition to measuring caspase-3 activity each time, at time zero, Banki et al. also measured caspase-3 activity at day 2, 4, 6 and 8—as shown in Figure 2; and at day 2, 4 and 7—as shown in Figure 5. Thus, not only did Banki repeat steps a) and b) numerous times, Banki et al. also measures caspase-3 activity at several time intervals.

With regard to the last bullet, Banki et al. clearly notes a repeat of the cell infection step at different times. See Figures 2 and 5, and particularly the last sentence of caption provided for the figures, pages 11946 and 11949, respectively. At the cited passage, Banki et al. notes that the data shown, which is the level of caspase-3 activity, is the mean +/- S.E. (standard error) of **four experiments**. With four different experiments conducted, it is clear that a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, and b)

measuring said caspase 3 activity were repeated numerous times. Furthermore, it should be noted that in addition to measuring caspase 3 activity at time zero, Banki et al. also measured caspase 3 activity at day 2, 4, 6 and 8, as shown by Figure 2; and day 2, 4 and 7, as shown by Figure 5 of Banki et al. Thus, in addition to repeating the process three more times, Banki et al. also collected the data at different time intervals. Hence, contrary to Appellant's assertion, Banki et al. does clearly teaches repeating the cell infection step using HIV obtained from a first formulation at different times.

In the instant case, contrary to Appellant's submission, it is clear that Banki et al. teaches a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, b) measuring said caspase 3 activity; and repeating steps a) and b) three times, with the HIV virus taken from Jurkat-tat and H9 cells, at several time intervals. Thus, Appellant's submission is not found persuasive.

In addition to above, Appellant submits that Banki et al. fails to provide motivation to modify Duncan et al. to look for at caspase 3 activity as an indication of viral activity. [Last paragraph, page 12 to page 13 of brief]

Appellant's submission has been considered, however, it is not found persuasive. In the instant case, Duncan et al. teaches two types of cells that are susceptible to apoptosis. The two cells that Duncan et al. teaches are Vero and RK13 cells. Duncan et al. further teaches a virus that induces apoptosis. The virus that Duncan et al. teaches is rubella virus. In summary, Duncan teaches that rubella virus induces apoptosis in Vero and RK13 cells. To quantify rubella-induced apoptosis in Vero and RK13 cells, Duncan et al. measured the number of detached cells. Duncan et al. does

not measure the level of caspase 3 activity to quantify apoptosis. It should be noted that Duncan et al. does recognize that caspase 3 activity are involved the process leading to apoptosis. [Third paragraph, first column, page 125 of Duncan et al.] Appellant also recognizes this latter point. [Last sentence, second paragraph under section B, page 13 of brief.]

However, the deficiency noted of Duncan et al. can readily be cured by Banki et al.

Banki et al. teaches an alternative method of quantifying apoptosis. In the instant case, Banki et al. teaches the measurement of caspase 3 activity to quantify apoptosis induced by a virus in a cell that is susceptible to caspase 3 activity. See Oxidative Stress Precedes Activation of Caspase-3 and PS Externalization during HIV-induced Apoptosis section, page 11948; and Figure 2 E and F, page 11946. At the cited passages, Banki et al. clearly teaches that increased caspase 3 activities occurred with a precipitous acceleration of cell death. [Last sentence, first paragraph of cited section, page 11948]

Hence, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to combine the teachings of Banki et al. with Duncan et al. One of ordinary skill in the art at the time the invention was made would have been motivated to so to quantify virally induced apoptosis. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the use of caspase 3 activity to quantify virally induced apoptosis is well known in the art.

Equivalently, in the instant case, Banki et al. teaches the measurement of caspase 3 activity to quantify viral induced apoptosis, as noted for claims 1-3. The virus and cells that Banki et al. teaches is HIV, Jurkat-tat and H9 cells, respectively. The virus and cells that Banki et al. teaches are not rubella virus and Vero and RK13 cells. In the instant case, it should be noted that Banki et al. teaches the measurement of caspase 3 activity to quantify to the extent of apoptosis induced by a virus in a cell that is susceptible to caspase 3 activity. See Oxidative Stress Precedes Activation of Caspase-3 and PS Externalization during HIV-induced Apoptosis section, page 11948; and Figure 2 E and F, page 11946. At the cited passages, Banki et al. clearly teaches that increased caspase 3 activities occurred with a precipitous acceleration of cell death. [Last sentence, first paragraph of cited section, page 11948]

As stated, the virus and cells that Banki et al. teaches are not rubella virus and Vero and RK13 cells. However, the deficiency noted of Banki et al. is fully compensated by the teachings of Duncan et al.

Duncan et al. teaches that that rubella virus induces apoptosis in Vero and RK13 cells.

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to combine the teachings of Banki et al. and Duncan et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so quantify rubella virus induced apoptosis in Vero and RK13 cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Duncan et al. teaches that

rubella virus induces apoptosis in Vero and RK13 cells, and Banki et al. teaches a method to quantify apoptosis by measuring caspase 3 activity.

Appellant also submits that the skilled artisan would not be motivated to modify Esolen et al. using the methods of employed by Banki et al. to determine the mechanism of measles virus-induced apoptosis because Esolen et al. does not reference caspase 3 activity as involved in cell death or indicate that caspase 3 activity should be quantified. [Second full paragraph, page 15 of brief.]

Appellant's submission has been considered, however, it is not found persuasive. While it may be true that Esolen et al. does not reference caspase 3 activity as involved in cell death or indicate that caspase 3 activity should be quantified; however, Appellant is reminded that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Banki et al. teaches a method of measuring caspase 3 activity to quantify virally induced apoptosis. Banki et al. also teaches that increased caspase 3 activity occurred with a precipitous acceleration in apoptosis of virally induced cells. While it is recognized that the virus that Banki et al. teaches is HIV, not measles or mumps. However, the deficiency noted of Banki et al. can be cured by the teachings of Esolen et al. Esolen et al. teaches a virus that induces apoptosis. The virus that Esolen et al. teaches is the measles virus. Esolen et

al. teaches that measles virus induces apoptosis. Hence, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to combine the teachings of Banki et al. and Esolen et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to quantify apoptosis induced by the measles virus. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the use of caspase 3 activity to quantify virally induced apoptosis is well known in the art.

For the reasons set forth above, Appellant's submission is not found persuasive.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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